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Thyroid gland metastasis arising from primary liver cholangiocarcinoma: The first case report involving surgical operation

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ABSTRACT

INTRODUCTION: A primary cancer causing thyroid metastasis is extremely rare. In western countries, the most common primary tumors causing thyroid metastases include kidney, lung, breast, and gastrointestinal cancers. In contrast, breast is the most common primary site, followed by kidney, colon, and lung cancers in Korea. To the best of our knowledge, surgically confirmed thyroid metastasis from cholangiocarcinoma has not been reported. Herein, we report the first case of thyroid metastasis secondary to cholangiocarcinoma on which surgery was performed.
PRESENTATION OF CASE: A 55-year-old man was diagnosed with hepatic malignancy in December 2008. He subsequently received 2 cycles of transarterial chemoembolization and 4 cycles of radio-frequency ablation between 2008 and 2010. At follow-up in January 2011, brain metastasis was identified in the right parietal area secondary to cholangiocarcinoma. In April 2011, the patient was found to have palpable masses on the left thyroid and lateral neck. The patient subsequently underwent total thyroidectomy followed by left radical neck dissection. Intraoperatively, an ill-defined mass measuring 6.0 cm was found infiltrating the subcutaneous tissue into the prevertebral fascia. Microscopic and immunohistochemical findings confirmed that the thyroid masses and lymph nodes were metastatic cholangiocarcinoma.
DISCUSSION: Positive immunohistochemical staining for cytokeratin 7, cytokeratin 19, and AFP and negative results for TG, TTF-1, and cytokeratin 20 can be definitely helpful in arriving at a correct diagnosis.
CONCLUSION: To the best of our knowledge, this is the first case report on surgically resected thyroid and lateral neck metastases secondary to cholangiocarcinoma.

1. Introduction

Metastasis to the thyroid gland secondary to other malignant tumors has been reported for a variety of primary tumors, but the condition remains extremely rare. In western countries, the most common primary tumors causing thyroid metastasis include kidney, lung, breast, and gastrointestinal cancers.[1,2] In contrast, breast is the most common primary site, followed by kidney, colon, and lung cancers in Korea.[3]

To the best of our knowledge, surgically confirmed thyroid metastasis from cholangiocarcinoma has not been reported. Although five cases of thyroid gland metastases have been reported secondary to hepatocellular carcinoma (HCC),[4–7] only one case report has been published on thyroid metastasis secondary to cholangiocarcinoma confirmed by fine needle aspiration cytology (FNAC), which was also reported by our institution.[8] Herein, we describe a male patient who developed concurrent brain and thyroid gland metastasis secondary to cholangiocarcinoma of the liver.

2. Presentation of case

A 55-year-old man was presumed to have hepatocellular carcinoma and not a type of cholangiocarcinoma in December 2008. Radiological examination revealed a 1.7 cm mass in segment 5 and a 4.0 cm mass in segment 6 of the liver (Fig. 1A). He had an elevated alpha-fetoprotein (AFP) of 2876 IU/mL (normal range = 0–5.8 IU/mL), but normal carcinoembryonic antigen (CEA; normal range = 0–4.7 ng/mL) and CA19-9 (normal range = 0–39 U/mL) levels. He subsequently received 2 cycles of transarterial chemoembolization (TACE) and 4 cycles of radio-frequency ablation (RFA) between 2008 and 2010.

At follow-up in January 2011, brain metastasis was identified in the right parietal area, which was assumed to be secondary to hepatocellular carcinoma. Intraoperatively, a mass measuring 2.7 cm × 2.6 cm × 2.0 cm was confirmed as cholangiocarcinoma and

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not hepatocellular carcinoma (Fig. 1B). No evidence of thyroid or lateral neck metastasis was found in a physical examination, radiological evaluation, and positron emission tomography (PET).

In April 2011, the patient was found to have palpable masses on the left side of the thyroid and lateral neck. Neck ultrasonography and computed tomography (CT) revealed a 6.0 cm × 3.4 cm mass on the left thyroid gland and multiple conglomerated, solid, and cystic metastatic lymphadenopathies on the left lateral neck. PET/CT showed solid and cystic lesions associated with left thyroid malignancy, exhibiting high fluorine-18 flurodeoxyglucose (FDG) uptake with a maximal standardized uptake value (SUVmax) of 13.4 in the thyroid and 10.3 in the left lateral neck with PET (Fig. 1C and D).

It was difficult to discern poorly differentiated thyroid carcinoma from metastatic liver malignancy by performing FNAC on the thyroid. However, we have presumed metastatic cholangiocarcinoma preoperatively on the thyroid and lateral neck, such as what was found in the brain. The patient subsequently underwent total thyroidectomy followed by left functional radical neck dissection. Intraoperatively, an ill-defined mass measuring 6.0 cm was found infiltrating the subcutaneous tissue into the prevertebral fascia.

Histopathological examination of the resected thyroid tissues and lymph nodes confirmed moderately differentiated adenocarcinoma (Fig. 2A), with microscopic characteristics similar to the brain lesions resected previously (Fig. 2B). Immunohistochemical studies were performed and displayed strong immunoreactivity for cytokeratin 7 and cytokeratin 19 and were negative for cytokeratin 20, thyroglobulin, thyroid transcription factor-1, hepatocyte-specific antigen, and α-fetoprotein (Fig. 3). Taken together, these microscopic and immunohistochemical findings confirmed that the thyroid masses and lymph nodes were metastatic cholangiocarcinoma.

3. Discussion

The incidence of thyroid metastases caused by all tumor types ranges between 1.9% and 9.5%.[9,10] Surgically resected thyroid metastasis specimens constitute between 0.02 and 1.4%.[11,12] Metastatic thyroid disease is found more frequently with the routine use of FNAB.[3] To the best of our knowledge, only one case of thyroid metastasis secondary to cholangiocarcinoma through the use of FNAB has been reported.[8] This is the first case of surgically resected thyroid metastasis due to cholangiocarcinoma.

The diagnosis of thyroid metastasis is frequently delayed because early symptoms and signs are subtle, and symptomatic thyroid dysfunction is rare. In patients with an oncological history of presenting with thyroid nodules, the possibility of thyroid metastasis should always be considered. However, it may be difficult to distinguish poorly differentiated thyroid carcinoma from

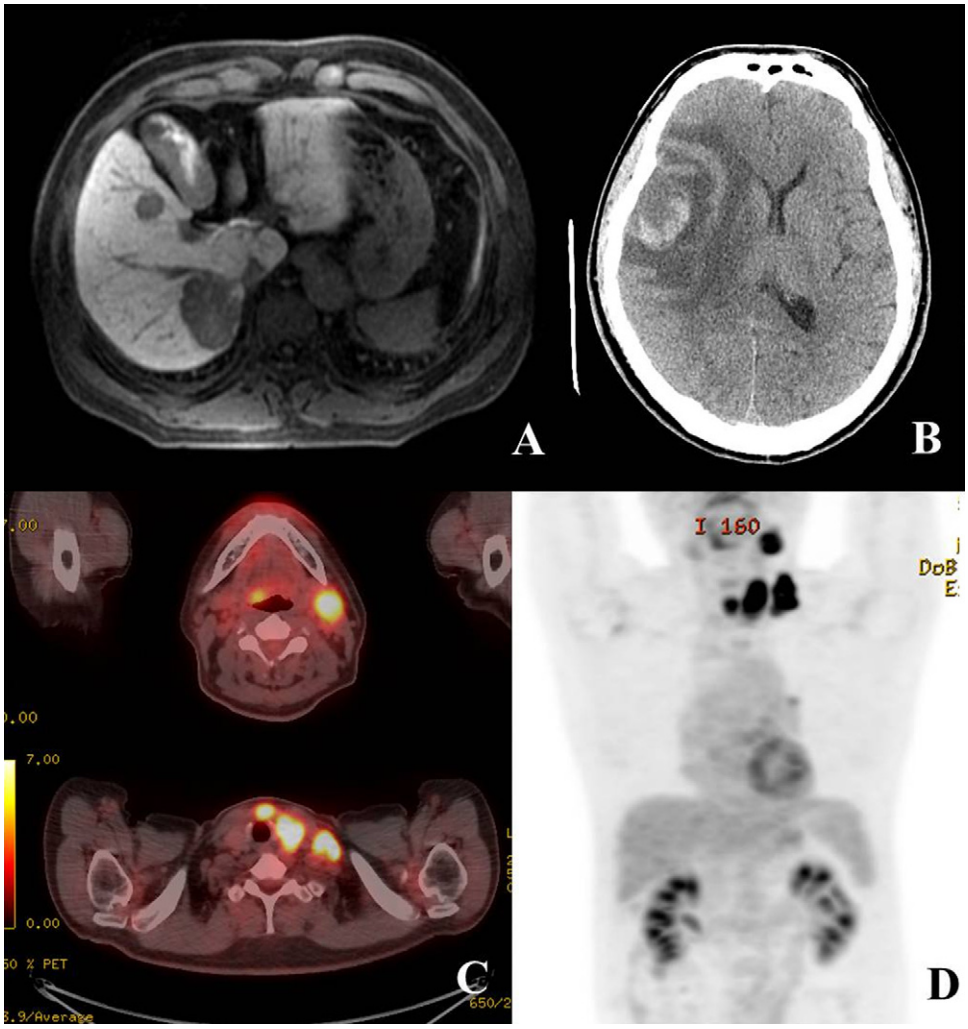

Fig. 1. Liver MRI shows 4.0 cm and 1.7 cm masses in the fifth and sixth segments of the right hepatic lobe, respectively, in December 2008 (A). CT shows a 2.7 cm × 2.6 cm × 2.0 cm metastatic cholangiocarcinoma in the right parietal area of the brain in January 2011 (B). F-18 FDG PET/CT in April 2011. PET/CT shows metastatic cholangiocarcinoma of 13.4 SUVmax in the left thyroid, isthmus, and multiple lymph nodes in the left lateral neck (C and D).

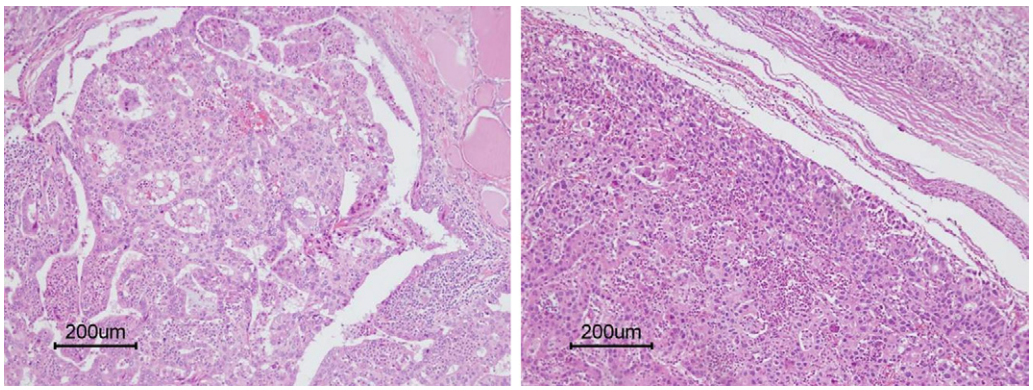

Fig. 2. Microscopically, malignant cells seen in the thyroid (A) and brain (B) showed the same histological features of cholangiocarcinoma. (H&E, 100×).

other metastatic thyroid malignancies. Thus, various immunohistochemical stains on pathological specimens may facilitate diagnosis.

A limitation of this case is that histological diagnosis was not performed on the pre-existing liver mass by percutaneous liver biopsy or other invasive methods. He underwent right hemicolectomy due to perforation of the hepatic flexure colon during percutaneous liver biopsy. Thus, the patient was presumed to have HCC or cholangiocarcinoma and underwent TACE and RFA treatment. The metastatic tumors in the brain and thyroid were completely matched with the microscopic histopathology of cholangiocarcinomas.

Our case of thyroid metastasis due to cholangiocarcinoma meets the criterion of histological appearance and also matches the immunohistochemical staining profile of cholangiocarcinomas. Cytokeratin 19 was positive in all cholangiocarcinomas and only in 5% of HCCs, and TTF-1 was identified in 93% of HCCs and 10% of cholangiocarcinomas.[13] In our case, positive immunohistochemical staining for cytokeratin 7, cytokeratin 19, and AFP and negative results for TG, TTF-1, and cytokeratin 20 can be definitely helpful in arriving at a correct diagnosis.

Aggressive surgical approaches with total or subtotal thyroidectomy and extensive lymph node dissection have been proposed.[14] Metastasis to the thyroid is rare, but most clinicians favor surgical resection to confirm the diagnosis and avoid local compressive symptoms, such as asphyxia. To date, however, no conclusive survival advantage following surgery has been proven.[2,14,15] Survival outcome, however, is universally poor with the diagnosis of thyroid metastasis and ranges between 1 and 12 months. The prognosis varies with the malignancy grade of the primary lesion and the presence of metastasis in organs other than the thyroid gland.[16] Chemotherapy has traditionally been administered as palliative treatment in this setting. Reports on chemotherapy for the treatment of thyroid metastases are scant, and the use of 5-FU alone in this setting yielded disappointing results, with survival ranging

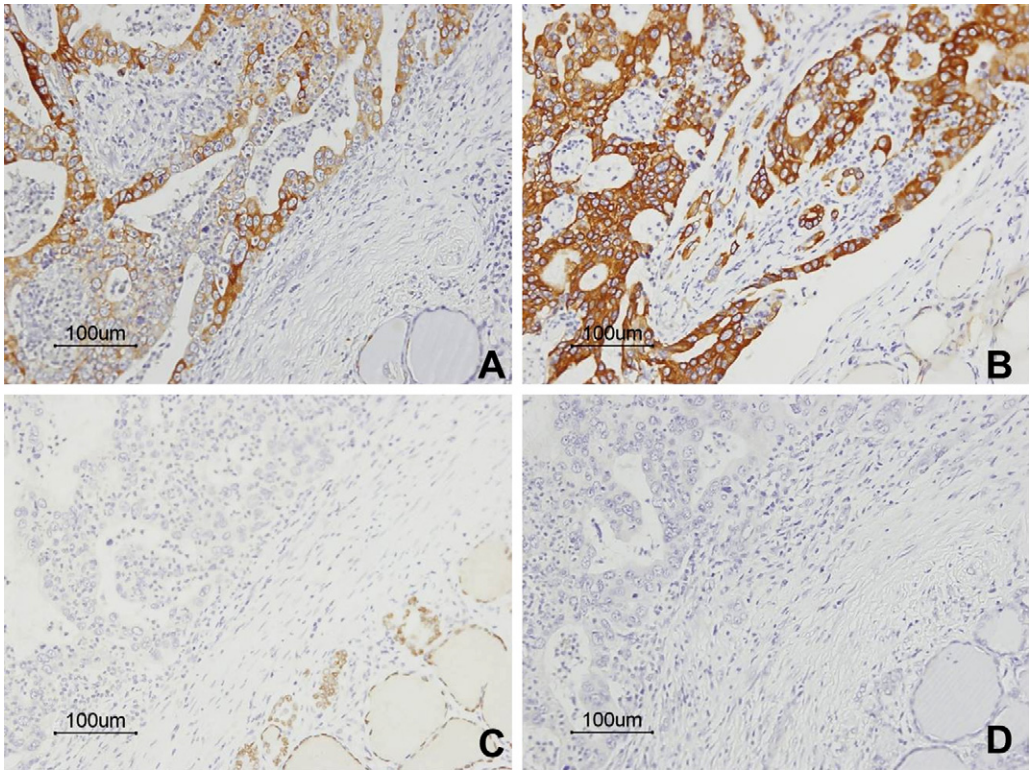

Fig. 3. Immunohistochemical features of cholangiocarcinoma metastasis to the thyroid. Tumor cells characteristically express cytokeratin 7 (A) and cytokeratin 19 (B), but do not express thyroid transcription factor-1 (C) and hepatocyte-specific antigen (D) (avidin-biotin-peroxidase, 200×).

between 1 and 6 months.[17,18] Two months after thyroidectomy with functional radical neck dissection, repeat CT showed local recurrence on the lateral neck bilaterally, for which the patient received 5-FU and platinum-based systemic chemotherapy.

4. Conclusion

To the best of our knowledge, this is the first case report on surgically resected thyroid and lateral neck metastases secondary to cholangiocarcinoma. Although uncommon, the possibility of a metastatic tumor involving the thyroid gland should always be considered in patients with oncological history.

Conflicts of interest

The authors declare no potential conflict of interest.

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None.

Consent and ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Prof. Min Ho Park, MD – 1st Author of case report, He performed the operation, involved in writing 1st draft.

Prof. Jin Seong Cho, MD – wrote up 2nd draft of the case report and analized current literature on the topic to format a discusstion, conclusion of the presented case.

Prof. Ji Shin Lee, MD – interpretation of histologic slides and provided the photomicrograph.

Prof. Hee Kyung Kim, MD – Contributed by revision it critically for intellectual consent.

Prof. Jung Han Yoon, MD – Consultant surgeon overseeing the case of this patient. He had final approval of the case report to be submitted.

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